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Please find below and/or attached an Office communication concerning this application or proceeding.

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/596,920
Filing Date: June 29, 2006
Appellant(s): VAN BOMMEL ET AL.

Kenneth D. Springer
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 7/20/2010 appealing from the Office action mailed 2/24/2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 15-33 are rejected and pending.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,818,199	HAINFELD	11-2004
2002/0103517	WEST	8-2002
2005/0020869	HAINFELD	1-2005

Bekeredjian, R. "Potential of Gold-bound Microtubule as a New Ultrasound Contrast Agent" *Ultrasound in Med. and Biol.*, vol 28, no. 5, (2002), pp. 691-695.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15-29, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hainfeld *et al.* (6,818,199), in view of .West *et al.* (US 2002/0103517).

Hainfeld discloses metal nanoparticles that are useful for enhancing the contrast of x-rays or other radiation sources (abstract). In a preferred form is a medical imaging method and contrast agent which contrasts a targeted portion of a body of a living animal. The method includes intravenously administering a quantity of nanoparticles sufficient to contrast the targeted portion of the body under irradiation and irradiating

the targeted portion of the body with penetrating radiation. Each of the nanoparticles has a metallic core surrounded by a surface layer including a component having an affinity for the targeted portion of the body (column 4, lines 53+). The metal nanoparticles have a core composed of gold, platinum, palladium, thallium, bismuth, osmium, iridium, silver, tungsten, lead, tantalum, or uranium. The component of the material of the surface layer may be for example, an antibody, an antibody fragment, a peptide, a lipid, a carbohydrate, a nucleic acid, or a drug (column 5, lines 1-10). One such preferred gold compound synthesized and found to be useful is a gold nanoparticle with a gold core approximately 2 nm in diameter, which contains about 240 gold atoms. "Metal particle" or "metal nanoparticle" are defined to be all constructs having a metal core ranging from 0.5 to 500 nm in size. "Gold particle" or "gold nanoparticle" are defined to be all constructs having a gold core ranging from 0.5 to 500 nm in size. Larger or smaller gold compounds, clusters, particles and colloids may also be utilized, e.g. gold colloids that are typically characterized by their gold diameter (from 0.5 nm to 100 nm) (column 6, lines 8-20). The outer surface shell of material may include a directing moiety or more than one directing moiety for specific targeting, such as an antibody, antibody fragment, peptide, lipid, carbohydrate, nucleic acid, drug, or other molecule. In addition, it is possible to couple further components to the shell material. By such means, the directing moieties such as antibodies or peptides may be attached. They may be directly coupled to the core by attachment through a sulfur atom, for example; alternatively they may be covalently coupled to the organic shell; additionally, they may be adsorbed non-covalently to the particle or particle shell

(column 9, lines 50+). In addition to x-rays, other forms of electromagnetic probes may be employed to detect or image the agents. This includes, but is not limited to, the use of: static magnetic fields, visible light, lasers, ultrasound (column 19, lines 10-15).

It is noted that the limitation of the instant claims wherein the particle has "an acoustic impedance above $35.1^5 \text{ g/cm}^2\text{s}$ " is not given patentable weight to distinguish over Hainfeld. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112. In the instant case, since Hainfeld teaches materials which have the same structural features as those claims, it is interpreted absent evidence to the contrary, that they would also have the claimed functional properties of acoustic impedance. This interpretation is supported by Applicant's specification, which teaches that acoustic impedance (Z) is defined as the product of density (ρ) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance

which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029).

Hainfeld does not specifically recite in vitro imaging. It is for this reason that West is joined.

West discloses localized delivery of heat and the localized imaging of biological materials. The delivery may be in vitro or in vivo and is useful for the localized treatment of cancer, inflammation or other disorders involving overproliferation of tissue. The method is also useful for diagnostic imaging (abstract). Nanoparticles include gold-containing nanoparticles (see claim 5). Methods of diagnostic imaging of cell or tissue comprising the steps of delivering nanoparticles to the cell or tissue and exposing said nanoparticles to radiation selected from the group consisting of ultrasound, magnetic fields, and electric fields are disclosed (see claim 33). With respect to instant claim 29, West discloses oral administration, including capsules.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the particles of Hainfeld for methods of in vivo or in vitro imaging when the teaching of Hainfeld is taken in view of West. Both Hainfeld and West are directed to gold-containing nanoparticles and methods of imaging/therapy, including ultrasound. West teaches that structurally similar particles are useful for in vivo and in vitro imaging, and one would have been motivated to use the particles of Hainfeld for in vitro imaging of cells and tissues in order to expand the applications for which the particles are useful. With respect to the limitation that diagnosis or imaging are achieved by applying an ultrasonic wave and receiving ultrasonic sound waves, such

steps would be inherent and necessary in the process of ultrasonic imaging disclosed in Hainfeld and/or West.

Claims 15-23, 25-28, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bekerredjian *et al.* (*Ultrasonnd in Med. and Biol.*, 2002, 28(5), p. 691-695).

Bekerredjian discloses gold-bound microtubules as ultrasound contrast agent. Gold colloid was immobilized on protein microtubule walls. Gold-bound microtubules provide a persistent contrast effect, suggesting their use as an ultrasonic contrast agent with the feasibility of antibody conjugation (abstract). Gold particles were 10 nm (page 692). With respect to instant claim 25, targeted drug delivery is also disclosed (page 695).

It would have been obvious to one of ordinary skill in the art at the time of the invention to extend the teachings of Bekerredjian to in vivo/in vitro ultrasonic imaging, since Bekerredjian specifically teaches that his compositions are intended for use as ultrasound contrast agents, and one would have had a reasonable expectation of success in doing so since Bekerredjian teaches that his compositions provide advantages such as a persistent contrast effect. With respect to the limitation that diagnosis or imaging are achieved by applying an ultrasonic wave and receiving ultrasonic sound waves, such steps would be inherent and necessary in the process of ultrasonic imaging (see page 692).

Claims 15-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hainfeld *et al.* (6,818,199), in view of West *et al.* (US 2002/0103517), further in view of Hainfeld *et al.* (US 2005/0020869).

The rejection over Hainfeld '199 in view of West is applied as above. It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute rhenium for gold, silver, etc. metal nanoparticles used in Hainfeld and/or West, when the teachings are taken in view of Hainfeld (US 2005/0020869).

Hainfeld (US 2005/0020869) teaches metal nanoparticles of 0.5 to 400 nm (abstract). Metals which can be used to form the metal nanoparticles include rhenium (paragraph 0019). For example, metals which can be used to form nanoparticles suitable for enhancing radiation effects are heavy metals, or metal with a high Z number, including but not limited to gold, silver, platinum, palladium, cobalt, iron, copper, tin, tantalum, vanadium, molybdenum, tungsten, osmium, iridium, rhenium, hafnium, thallium, etc. (paragraph 0019-20). Forms of energy suitable for interaction with the particles includes ultrasound (paragraph 0116).

Accordingly, Hainfeld '199, West and Hainfeld (US 2005/0020869) are drawn to high z metal nanoparticles. The use of such particles for use in diagnostic imaging, including x-ray, ultrasound, etc is disclosed in Hainfeld '199 and West. One of ordinary skill could have substituted one known high z metal nanoparticle (e.g. rhenium for gold, silver, etc.) for use in imaging methods of Hainfeld and/or West, including ultrasonic imaging, and the result would have been predictable, since Hainfeld (US

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2005.0020869) teaches rhenium to be functionally equivalent to gold and other metal nanoparticles, including for interaction with forms of energy including ultrasound.

(10) Response to Argument

With regard to the rejection under 35 U.S.C. 103(a) over Hainfeld (US 6,818,199) in view of West (US 2002/0103517), Applicant argues on pages 3-7 of the Appeal Brief that the Examiner has failed to meet the burden showing that a feature of receiving ultrasound wave reflections produced by an ultrasonic wave in an animal or human subject, including ultrasound wave reflections from solid metal nanoparticles having an acoustic impedance of $35 \times 10^5 \text{ g/cm}^2\text{s}$ is necessarily present in the teachings of Hainfeld I or West. Applicant argues that Hainfeld I explicitly lists forms of electromagnetic radiation, and that one can only conclude that by plain language of col. 19, lines 10-15, and the context presented by the remainder of Hainfeld's disclosure that Hainfeld is referring to low frequency electromagnetic waves. Applicant further argues that there is no disclosure or suggestion in Hainfeld I of the acoustic properties (e.g. acoustic impedance) of the nanoparticles that Hainfeld I discloses, and that it is not reasonable to interpret the cited language in col. 19 of Hainfeld I as pertaining to acoustic waves and Hainfeld I does not inherently teach receiving ultrasound sound wave reflections from solid metal nanoparticles having an acoustic impedance above $35 \times 10^5 \text{ g/cm}^2\text{s}$. Applicant further argues that West does not disclose that imaging is performed from ultrasound reflections from the nanoshells.

This is not found to be persuasive. It is clear from Hainfeld that the metal nanoparticles may be used for diagnostic imaging, including via ultrasound, and that one skilled in the art will be familiar with the use of sources other than x-rays to produce detection or imaging of metal particles (column 19). With regard to Hainfeld, it is

acknowledged that ultrasonic sonic waves are not formally classified as being an electromagnetic probe. However, Hainfeld specifically recites ultrasound in conjunction with "x-rays, other forms of electromagnetic probes may be employed to *detect or image the agents*," and includes ultrasound. Applicant's assertion that Hainfeld is referring to "low frequency electromagnetic waves" is not found to be persuasive because Hainfeld specifically recites ultrasound, and also because ultrasound is disclosed in the context of imaging/diagnostics. Ultrasound is known in the in vivo diagnostic arts via use of contrast agents, and "low frequency electromagnetic waves," as alleged by Applicant, are not. This interpretation is further supported by Hainfeld's patent US 5,360,895, drawn to gold clusters (nanoscale) which states that gold can be detected in ultrasonic imaging (column 4, line 43). As set forth in the rejection, ultrasound imaging would necessarily require applying and receiving ultrasound waves. West also teaches diagnostic imaging with ultrasound (see especially paragraph 0027 and claim 33). With regard to the claimed physical property of acoustic impedance associated with metal nanoparticles, the examiner asserts that acoustic impedance is a measurable physical property of a given material. Applicant's specification, discloses that acoustic impedance (Z) is defined as the product of density (ρ) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029). The gold nanoparticles in the compositions of Hainfeld inherently have the requisite density, since they are nanoparticles of the same materials as those which are claimed. Absent

evidence to the contrary, the particles would also have the same acoustic impedance. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Regarding the rejection under 35 U.S.C. 103(a) over Bekerredjian (Ultrasound in Med. and Biol, 2002, 28(5), p. 691-695), Applicant argues on pages 7-8 of the Appeal Brief that Bekeedjian does not disclose or suggest administering solid metal nanoparticles having an acoustic impedance above $35 \times 10^5 \text{ g/cm}^2\text{s}$. Applicant argues that instead, Bekerredjian discloses attaching gold colloids to the walls of microtubules and administering the colloidal gold-bound microtubules as the contrast agent. Applicant asserts that administering colloidal gold-bound microtubules is not administering solid metal nanoparticles having an acoustic impedance above $35 \times 10^5 \text{ g/cm}^2\text{s}$.

This is not found to be persuasive. It is noted that the comprising language of the instant claims does not preclude the presence of microtubules. The instant claims recite "administering a contrast agent *comprising solid metal nanoparticles* having an acoustic impedance above 35.10 g/cm^2 to an animal or human subject...". In the case of the Bekerredjian reference the contrast agent comprises proteinaceous microtubules having 10 nm gold particles bound thereto (see page 692, left column). The gold nanoparticles are solid. With regard to the claimed physical property of acoustic

impedence associated with metal nanoparticles, the examiner asserts that acoustic impedance is a measurable physical property of a given material. Applicant's specification, discloses that acoustic impedance (Z) is defined as the product of density (ρ) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029). The gold nanoparticles in the compositions of Bekeradjian inherently have the requisite density, since they are nanoparticles of the same materials as those which are claimed. Absent evidence to the contrary, the particles would also have the same acoustic impedance. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The examiner respectfully submits that the instant claim language is readable upon contrast agents comprising both (solid) gold nanoparticles and proteinaceous microtubules.

With regard to the rejection under 35 U.S.C. 103(a) over Hainfeld (US 6,818,199) in view of West (US 2002/0103517), in further view of Hainfeld (US 2005/0020869), Applicant argues on pages 8-11 of the Appeal Brief that claims 30 and 31 include receiving ultrasound sound wave reflections produced by an ultrasonic wave in an

animal or human subject, including ultrasound sound wave reflections from solid rhenium nano- particles having an acoustic impedance above $35 \times 10^5 \text{ g/cm}^2\text{s}$.

Applicants respectfully submit that Hainfeld I, West and Hainfeld II, taken alone or collectively, do not teach any method including such a combination of features.

Applicant argues that Hainfeld II is concerned with enhancing the effectiveness of electromagnetic radiation therapy, not imaging. Therefore, Hainfeld II is concerned with a particular characteristic of how its particles interact with electromagnetic radiation, namely the radiation absorption rate of the material. Hainfeld II does not mention anything about how its particles interact with acoustic radiation, for example the acoustic impedance of the particles. Applicants respectfully submit that Hainfeld II does not teach or suggest the use of solid rhenium nano-particles in ultrasonic imaging. Instead, Hainfeld II only teaches the use of nanoparticles made from rhenium in a therapeutic application to enhance energy delivery.

This is not found to be persuasive. Hainfeld II teaches that rhenium and other metal nanoparticles are capable of interaction with various energy sources, including ultrasound. One of ordinary skill would have had a reasonable expectation of success in using rhenium nanoparticles as equivalent to gold nanoparticles in diagnostic ultrasound imaging since Hainfeld II teaches rhenium, gold and other metals to be capable of interaction with ultrasound energy and Hainfeld I and West teach diagnostic imaging with metal nanoparticles, including ultrasound, and West teaches ultrasound is known for therapeutic or diagnostic applications (see West paragraph 0027). Since rhenium shown to be equivalent to other metals for interaction with ultrasound, and

ultrasound is known to be used for therapeutic or diagnostic applications using metal nanoparticles as contrast agent, one of ordinary skill would have had a reasonable expectation of success in performing therapeutic or diagnostic ultrasound with rhenium nanoparticles.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Conferees:

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